Principles of rational haemotherapy

Complications of blood transfusion

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HEMOTHERAPY = treatment of a patient by means of substitution of blood or blood components and fractionated plasma products.

TRASFUSION = administration of blood components or FFP obtained from a donor to the bloodstream of a recipient.
PRINCIPLES

- transfusion just of these blood components which patient really need

- treatment of clinical symptoms, not laboratory results

- consider: the risk of not transfusing a patient

  X

  the risk of adverse reaction to BT
Effective use of blood components

Decision-making about application of blood components

• patient’s symptoms, diagnosis, co-morbidity
• laboratory results
• planned treatment
• possibility of alternatives to transfusion
• availability of blood components
• recommendation in the institute
• evidence-based medicine
red cell concentrates

platelets

fresh frozen plasma

granulocytes

indications / contraindications
Transfusion of red cells

Acute blood loss

The transfusion trigger is **Hb 70-80 g/l** for young patients and **100 g/l** for older patients and patients with co-morbidity, individual assessment.

„A restrictive strategy of red-cell transfusion is at least as effective and possibly superior to a liberal transfusion strategy in critically ill patients, with possible exception of patients with acute myocardial infarction and unstable angina.“ (TRICC Study, N Eng J Med 1999)

Massive transfusion protocol  E:P:T in ratio 4:4:1
**Chronic anemia**

- patients without cardiovascular disease - **Hb < 70 g/l**

- patients with cardiovascular disease or respiratory disease - **Hb < 90-100 g/l**
Transfusion of platelets

INDICATIONS

- indicated for prevention and treatment of hemorrhage by patients with thrombocytopenia or platelet function defects

- supportive care for patients treated with myeloablative chemotherapy

- prophylactic before invasive procedures by thrombocytopenic patients
PROPHYLACTIC PLATELET TRANSFUSION

- risk of bleeding: \(< 10 \times 10^9/l\)

- other complications (fever, sepsis, coagulopathy) 
  \(< 20 \times 10^9/l\)
INVASIVE PROCEDURES

- teeth extraction: $> 30 \times 10^9/l$
- insertion of indwelling catheter: $> 50 \times 10^9/l$
- lumbar puncture, epidural anaesthesia, gastroscopy and biopsy, transbronchial biopsy, laparotomy or similar procedures, delivery – C-section: $> 50 \times 10^9/l$
- major surgery: $> 70 \times 10^9/l$
- surgery in critical organs (brain or eyes): $> 100 \times 10^9/l$
- several days after surgery $> 50 \times 10^9/l$
Transfusion of platelets

**INDICATIONS**

- Massive acute blood loss > 50x10^9/l
  - dilute thrombocytopenia caused by massive transfusion
- DIC > 50x10^9/l
- Bleeding + brain injury > 100x10^9/l

**Autoimmune thrombocytopenia - ITP**
- only for patients with major bleeding

**Thrombotic thrombocytopenic purpura – TTP**
- KI of platelet transfusion

⇒ the cause of thrombocytopenia should be established before a decision about the use of platelet transfusion!
Indications for Transfusion of FFP:

- To replace rare clotting factor deficiencies for which no virus-safe fractionated product is available.

- To treat multifactor deficiency due to severe bleeding and disseminated intravascular coagulation.

- For correction of clinically significant (bleeding, invasive procedure) over-anticoagulation due to warfarin.

- In case of thrombotic thrombocytopenic purpura (plasma exchange).
Transfusion of granulocytes

INDICATIONS

therapeutic indication

- sepsis or local infection not responding to adequate antimicrobial therapy (antibiotics, antifungal drugs) in neutropenic patient with chemosensitive hematologic malignancy together with neutrophil count $< 0.5 \times 10^9/\text{l}$ or neutrophil dysfunction

prophylactic indication? (generally not recommended)

- after allogenic BM/SC transplantation as primary prevention of infection or secondary prevention - prevention of recurrence of infection
Evo, tohle není salát, ale můj koš se špinavým prádlem...
Complications of transfusion
Complications of transfusion

**immune complications**
- hemolytic transfusion reaction
- febrile non-hemolytic transfusion reaction
- transfusion-related acute lung injury (TRALI)
- transfusion-induced graft versus host disease
- anaphylaxis and anaphylactoid reaction
- posttransfusion purpura
- alloimmunization
- immunomodulation

**transfusion transmitted infections and bacterial contamination**
- viral (HBV, HVC, HIV), bacterial (syphilis), parasites, prions

**cardiovascular and metabolic complications**
- circulatory overload, hypothermia, hyperkalaemia, hypokalcemia, citrate toxicity, hypotension, hypertension, iron overload - hemosiderosis
Immune complications

Haemolytic transfusion reaction

- **Acute** = during or within 24 hours after the transfusion intravascular haemolysis
- **Delayed** = 5-10 days following the transfusion extravascular haemolysis
donor cells with "foreign" antigens + recipient specific antibodies (existing/produced) → binding antibody to antigen →
- phagocytosis
- fragmentation
- ADCC

• intravascular hemolysis (complement activation up to MAC)
• Release of cytokines – TNF, IL-1, IL-6, IL-8
Immune complications

**Acute hemolytic transfusion reaction**  - AB0 incompatibility

**S&S:** fever, chills or both, pain, hypotension, tachycardia or both, agitation and confusion, particularly in the elderly nausea or vomiting, dyspnoea, flush, hemoglobinuria

**COMPLICATIONS:** renal failure (ATN), DIC, death

**MANAGEMENT:** stop the transfusion, check patient identity, monitor pulse, blood pressure and temperature at 15 minute intervals, maintain adequate renal perfusion (fluid, furosemid, dopamin) and monitor blood clotting tests.

**Always send a blood sample and the transfusion pack to the Transfusion service for re-examination!**
**Immune complications**

**Delayed hemolytic transfusion reaction**
(non-AB0 incompatibility – Rh, Kidd, Duffy, Kell..)

- several days after transfusion (5 – 10 days)

- secondary immune response following re-exposure to a given red cell Ag (pregnancy, previous blood transfusion)

- alloAb may be undetectable in the patient plasma prior to BT

**S&S:** fever, ↓ hemoglobin, mild icterus (hemoglobinuria)

**LAB.:** DAT+, new alloantibody detection

**MANAGEMENT:** no therapy; monitoring of renal functions
Immune complications

**febrile non-hemolytic transfusion reaction (FNHTR)**

= T rise of > 1 °C without obvious cause within or after BT

- a common adverse reaction to blood transfusion

**PATHOGENESIS:** pyrogenic cytokines (IL-1, IL-6, TNF) released from donor WBCs either after the contact with recipient anti-Leu antibodies or during the platelet storage

→ **leucocyte depletion** of blood components is effective in prevention of FNHTRs

**DIF. DG.:**

- acute hemolytic reaction
- transfusion-transmitted bacterial infection
- fever unrelated to blood transfusion
TRALI (transfusion related acute lung injury) = a severe acute pulmonary reaction associated with the transfusion of blood containing donor plasma

-occurs infrequently, but is one of the commonest causes of death associated with blood transfusions

S&S: acute respiratory distress, hypoxia, pulmonary infiltrates and severe pulmonary oedema soon after transfusion with no other apparent cause

PATHOGENESIS: HLA or granulocyte specific antibodies in donor plasma causing recipient leucocytes activation resulting in pulmonary leucostasis, capillary leak and pulmonary damage

MANAGEMENT: prompt respiratory support
Anaphylaxis and allergic reactions

**anaphylaxis**
- is a life threatening allergic reaction
- IgA deficit separately or together with IgA antibodies

**S&S:** severe breathing difficulty, shock, arrhythmias, loss of consciousness

**anaphylactoid reactions**
- IgE independent and can occur on first exposure

**mild allergic reactions**
- common; local cutaneous reactions or chest tightness

**MANAGEMENT:** hydrocortizon, antihistaminics, adrenaline
Immune complications

**TA-GVHD**

- the commonest transfusion-related cause of death reported to the UK Serious Hazards of transfusion scheme
- the incidence is low, but treatment is not effective

**S&S:** the classical features of skin rash, diarrhoea and liver dysfunction followed by bone marrow hypoplasia, pancytopenia and death from infection within 3-4 weeks of transfusion

**PATHOGENESIS:** alloreactive lymphocytes proliferation – direct lymfocytotoxicity and the cytokine response

**PREVENTION:** γ-irradiation of blood components to a dose of 25 Gy in high risk situation (immunocompromised patients, transfusion of granulocytes, transfusions between family members)
Irradiation

reason

- ↓ risk of TA-GVHD in immunocompromised patients

indications for administration of irradiated blood components

- transplanted patient
- transfusion from relatives or HLA compatible donors
- intrauterine and neonate transfusion
- severe immunocompromised patients
Transfusion transmitted infections

Transfusion transmissable infectious agents

**viruses** (HAV, HBV, HCV, HIV, CMV, EBV, HHV 8, Parvovirus B19)
**bacteria** (Treponema pallidum, Borrelia burgdorferi, Yersinia enterocolica, Pseudomonas aeruginosa, Staphylococcus sp.)
**protozoa** (Plasmodium, Trypanosoma, Toxoplasma gondii)
**prions** (cause CJD)

**PREVENTION:** donor selection, screening of all donations for selected pathogens (serology, PCR), FFP quarantine, good manufacturing practice, leukocyte depletion, pathogen inactivation
Leucocyte depletion

reasons

• ↓ occurrence of adverse reactions - FNHTRs
• ↓ risk of alloimmunisation
• ↓ risk of transmission of CMV

indication

• repeated adverse reaction – FNHTRs
• presence of anti-HLA antibodies
• often transfused patients
• transplanted patients (or other immunocompromised)
• intrauterine and neonate transfusion, pregnant women
Thank you for your attention